GenCore version 4.5


OM protein - protein search, using sw model

Run on: June 21, 2002, 08:23:31 ; Search time 93.48 Seconds
(without alignments)
103.374 Million cell updates/sec

Title: US-09-351-778A-10
Perfect score: 87
Sequence: 1 MTGSTIAPTTDYRNTTATGL.....RPPIYRPIGLKPCSLLLQYD 87

Scoring table: OLIGO
Gapop 60.0 , Gapext 60.0

Searched: 747574 seqs, 111073796 residues

Word size : 0

Total number of hits satisfying chosen parameters: 747574

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Listing first 45 summaries

Database : A_Geneseq_032802:*
1: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS1/gcgdata/hold-geneseq/geneseqp-embl/AA2001.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | % Query Match | Length | DB | ID | Description |
|---|---|---|---|---|---|---|
| 1 | 87 | 100.0 | 87 | 22 | AAB61870 | Ad2 ADP mutant dl7 |
| 2 | 75 | 86.2 | 78 | 22 | AAB61869 | Ad2 ADP mutant dl7 |
| 3 | 75 | 86.2 | 101 | 19 | AAW78902 | Adenovirus death p |
| 4 | 75 | 86.2 | 101 | 19 | AAW75787 | Adenovirus death p |
| 5 | 75 | 86.2 | 101 | 19 | AAW61197 | Adenovirus death p |
| 6 | 75 | 86.2 | 101 | 20 | AAW98003 | Adenovirus death p |
| 7 | 75 | 86.2 | 101 | 21 | AAY84407 | Amino acid sequenc |
| 8 | 75 | 86.2 | 101 | 22 | AAB47591 | ADP amino acid seq |
| 9 | 75 | 86.2 | 101 | 22 | AAM50206 | Adenovirus death p |
| 10 | 75 | 86.2 | 101 | 22 | AAB61866 | Ad2 encoded adenov |
| 11 | 70 | 80.5 | 77 | 22 | AAB61871 | Ad2 ADP mutant dl7 |
| 12 | 52 | 59.8 | 101 | 19 | AAW59925 | Adenovirus death p |
| 13 | 40 | 46.0 | 40 | 22 | AAB61873 | Ad2 ADP putative l |
| 14 | 35 | 40.2 | 95 | 22 | AAB61868 | Ad6 encoded adenov |
| 15 | 30 | 34.5 | 84 | 22 | AAB61872 | Ad2 ADP mutant dl7 |
| 16 | 24 | 27.6 | 93 | 22 | AAB61867 | Ad5 encoded adenov |
| 17 | 19 | 21.8 | 19 | 22 | AAB61874 | Ad2 ADP transmembr |
| 18 | 18 | 20.7 | 94 | 22 | AAB61865 | Ad1 encoded adenov |
| 19 | 16 | 18.4 | 42 | 22 | AAB61876 | Ad2 ADP cytosolic |
| 20 | 8 | 9.2 | 8 | 22 | AAB61875 | Ad2 ADP cytosolic |
| 21 | 7 | 8.0 | 157 | 21 | AAG18744 | Zea mays protein f |
| 22 | 7 | 8.0 | 197 | 20 | AAY34853 | C. pneumoniae cell |
| 23 | 7 | 8.0 | 197 | 22 | AAU43319 | Propionibacterium |
| 24 | 7 | 8.0 | 242 | 21 | AAG04903 | Arabidopsis thalia |
| 25 | 7 | 8.0 | 242 | 21 | AAG59416 | Arabidopsis thalia |
| 26 | 7 | 8.0 | 273 | 22 | ABG05846 | Novel human diagno |
| 27 | 7 | 8.0 | 316 | 21 | AAG04902 | Arabidopsis thalia |
| 28 | 7 | 8.0 | 316 | 21 | AAG59415 | Arabidopsis thalia |
| 29 | 7 | 8.0 | 404 | 22 | ABB65340 | Drosophila melanog |
| 30 | 7 | 8.0 | 473 | 22 | ABG26845 | Novel human diagno |
| 31 | 7 | 8.0 | 482 | 21 | AAY96786 | Soybean sucrose no |
| 32 | 7 | 8.0 | 604 | 22 | ABB67946 | Drosophila melanog |
| 33 | 7 | 8.0 | 635 | 22 | ABB66261 | Drosophila melanog |
| 34 | 6 | 6.9 | 15 | 22 | AAG78731 | Human copper/zinc |
| 35 | 6 | 6.9 | 43 | 22 | ABB44015 | Peptide #11521 enc |
| 36 | 6 | 6.9 | 43 | 22 | AAM65030 | Human brain expres |
| 37 | 6 | 6.9 | 43 | 22 | AAM77745 | Human bone marrow |
| 38 | 6 | 6.9 | 43 | 22 | AAM21656 | Peptide #8090 enco |
| 39 | 6 | 6.9 | 43 | 22 | AAM37959 | Peptide #11996 enc |
| 40 | 6 | 6.9 | 50 | 22 | AAB78805 | Deadpan mutant bHL |
| 41 | 6 | 6.9 | 50 | 22 | AAB78832 | Deadpan mutant bHL |
| 42 | 6 | 6.9 | 51 | 22 | AAB78806 | Deadpan mutant bHL |
| 43 | 6 | 6.9 | 51 | 22 | AAB78831 | Deadpan mutant bHL |
| 44 | 6 | 6.9 | 52 | 22 | AAU48951 | Propionibacterium |
| 45 | 6 | 6.9 | 52 | 22 | AAB78807 | Deadpan mutant bHL |

ALIGNMENTS

RESULT 1
AAB61870
ID AAB61870 standard; Protein; 87 AA.
XX
AC AAB61870;
XX
DT 08-MAY-2001 (first entry)
XX
DE Ad2 ADP mutant dl715.
XX
KW Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW anti-cancer; gene therapy; cytostatic; Ad2; mutant.
XX
OS Mastadenovirus.
XX
PN WO200104282-A2.
XX
PD 18-JAN-2001.
XX
PF 12-JUL-2000; 2000WO-US18971.
XX
PR 12-JUL-1999; 99US-0351778.
XX
PA (UYSL-) UNIV SAINT LOUIS.
XX
PI Wold WSM, Toth K, Doronin K, Tollefson AE;
XX
DR WPI; 2001-103079/11.
XX
PT Recombinant vector which is replication-competent in a neoplastic cell
PT and overexpresses an adenovirus death protein, useful in cancer therapy
PT when used together with replication-defective adenovirus which
PT expresses an anti-cancer gene -
XX

PS Example 9; Fig 20; 196pp; English.
XX
CC The invention relates to a recombinant vector (V1) which is replication-
CC competent in a neoplastic cell and which overexpresses an adenovirus
CC death protein (ADP). The vector can be used in a method for promoting
CC death of a neoplastic cell that comprises contacting the neoplastic cell
CC with at least one V1; and a composition comprising V1 and a second
CC recombination virus which is: (a) replication defective and which
CC expresses an anti-cancer gene product, where V1 complements replication
CC of the second recombinant virus; or (b) replication-competent in a
CC neoplastic cell. V1, together with one or more replication-defective
CC adenovirus which expresses an anti-cancer gene product, are useful in
CC cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC cells and spread of the virus throughout a cell monolayer than viruses
CC expressing wild-type levels of ADP. The present sequence represents the
CC amino acid sequence of an Ad2 ADP mutant.
XX
SQ Sequence 87 AA;

Query Match 100.0%; Score 87; DB 22; Length 87;
Best Local Similarity 100.0%; Pred. No. 9.6e-81;
Matches 87; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy 61 CLKRRRARPPIYRPIGLKPCSLLLQYD 87
|||||||||||||||||||||||||||
Db 61 clkrrrarppiyrpiglkpcslllqyd 87

RESULT 2
AAB61869
ID AAB61869 standard; Protein; 78 AA.
XX
AC AAB61869;
XX
DT 08-MAY-2001 (first entry)
XX
DE Ad2 ADP mutant dl716.
XX
KW Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW anti-cancer; gene therapy; cytostatic; Ad2; mutant.
XX
OS Mastadenovirus.
XX
PN WO200104282-A2.
XX
PD 18-JAN-2001.
XX
PF 12-JUL-2000; 2000WO-US18971.
XX
PR 12-JUL-1999; 99US-0351778.
XX
PA (UYSL-) UNIV SAINT LOUIS.
XX
PI Wold WSM, Toth K, Doronin K, Tollefson AE;
XX
DR WPI; 2001-103079/11.
XX
PT Recombinant vector which is replication-competent in a neoplastic cell
PT and overexpresses an adenovirus death protein, useful in cancer therapy
PT when used together with replication-defective adenovirus which
PT expresses an anti-cancer gene -
XX
PS Example 9; Fig 20; 196pp; English.
XX
CC The invention relates to a recombinant vector (V1) which is replication-
CC competent in a neoplastic cell and which overexpresses an adenovirus
CC death protein (ADP). The vector can be used in a method for promoting
CC death of a neoplastic cell that comprises contacting the neoplastic cell
CC with at least one V1; and a composition comprising V1 and a second
CC recombination virus which is: (a) replication defective and which
CC expresses an anti-cancer gene product, where V1 complements replication
CC of the second recombinant virus; or (b) replication-competent in a
CC neoplastic cell. V1, together with one or more replication-defective
CC adenovirus which expresses an anti-cancer gene product, are useful in
CC cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC cells and spread of the virus throughout a cell monolayer than viruses
CC expressing wild-type levels of ADP. The present sequence represents the
CC amino acid sequence of an Ad2 ADP mutant.
XX
SQ Sequence 78 AA;

Query Match 86.2%; Score 75; DB 22; Length 78;
Best Local Similarity 100.0%; Pred. No. 1.4e-68;
Matches 75; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy 61 CLKRRRARPPIYRPI 75
|||||||||||||||
Db 61 clkrrrarppiyrpi 75

RESULT 3
AAW78902
ID AAW78902 standard; Protein; 101 AA.
XX
AC AAW78902;
XX
DT 21-DEC-1998 (first entry)
XX
DE Adenovirus death protein.
XX
KW Carcinoembryonic antigen; transcriptional regulatory element;
KW CEA-TRE; human; promoter; enhancer; vector; cancer; gene therapy;
KW PCR; primer; adenovirus death protein; ADP.
XX
OS Mastadenovirus.
XX
PN WO9839467-A2.
XX
PD 11-SEP-1998.
XX
PF 03-MAR-1998; 98WO-US04133.
XX
PR 02-MAR-1998; 98US-0039763.
PR 03-MAR-1997; 97US-0039763.
XX
PA (CALY-) CALYDON INC.
XX
PI Henerson DR, Lamparski HG, Schuur ER;
XX
DR WPI; 1998-495862/42.
DR N-PSDB; AAV52966.
XX
PT New adenovirus vectors, particularly for cancer therapy - comprising
PT adenovirus gene under transcriptional control of carcinoembryonic
PT antigen transcriptional regulatory element
XX
PS Disclosure; Page 68; 95pp; English.
XX
CC This is the amino acid sequence of adenovirus death protein (ADP).
CC Claimed replication-competent adenovirus (Ad) vectors comprise an
CC Ad gene under transcriptional control of a CEA-TRE. The vectors can
CC be used to detect and monitor samples for the presence of cells that
CC allow a CEA-TRE to function, and to selectively kill such cells,
CC especially malignant cells. Vectors containing an ADP gene (see
CC AAV52966) may be more potent than vectors lacking the gene, making
CC possible more effective treatment and/or lower dosage requirement.

```
XX
SQ   Sequence   101 AA;

  Query Match           86.2%;  Score 75;  DB 19;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy     61 CLKRRRARPPIYRPI 75
          |||||||||||||||
Db     61 clkrrrarppiyrpi 75


RESULT   4
AAW75787
ID   AAW75787 standard; Protein; 101 AA.
XX
AC   AAW75787;
XX
DT   21-DEC-1998  (first entry)
XX
DE   Adenovirus death protein.
XX
KW   Probasin transcriptional response element; PB-TRE; rat;
KW   androgen receptor; adenovirus; vector; prostate cancer;
KW   gene therapy; adenovirus death protein; ADP.
XX
OS   Mastadenovirus.
XX
PN   WO9839466-A2.
XX
PD   11-SEP-1998.
XX
PF   03-MAR-1998;   98WO-US04132.
XX
PR   02-MAR-1998;   98US-0033333.
PR   03-MAR-1997;   97US-0039762.
XX
PA   (CALY-) CALYDON INC.
XX
PI   Henderson DR,  Lamparski HG,  Schuur ER,  Yu D;
XX
DR   WPI; 1998-506369/43.
DR   N-PSDB; AAV57354.
XX
PT   New adenovirus vectors, particularly for cancer therapy - comprising
PT   an adenovirus gene under transcriptional control of a probasin
PT   transcriptional regulatory element
XX
PS   Disclosure; Page 96; 117pp; English.
XX
CC   This is the amino acid sequence of adenovirus death protein (ADP).
CC   Claimed replication-competent adenovirus (Ad) vectors comprise an
CC   Ad gene under transcriptional control of a probasin transcriptional
CC   response element (PB-TRE, see AAV57334).  The vector can be used for
CC   detecting cells that allow a PB-TRE to function, especially cells
CC   expressing an androgen receptor, such as prostate cells.  They can
CC   be used to confer selective toxicity to such cells.  In particular,
CC   the vectors can be used for treating cancers such as prostate cancer.
CC   Ad vectors containing the ADP gene (see AAV57354) may render the
CC   vector more potent, making possible more effective treatment and/or
CC   a lower dosage requirement.  An Ad vector has been constructed that
CC   contains the ADP gene under control of PB-TRE.  Cytotoxicity was
CC   demonstrated toward LNCaP (prostate carcinoma) cells.
XX
SQ   Sequence   101 AA;

  Query Match           86.2%;  Score 75;  DB 19;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy     61 CLKRRRARPPIYRPI 75
          |||||||||||||||
Db     61 clkrrrarppiyrpi 75


RESULT   5
AAW61197
ID   AAW61197 standard; Protein; 101 AA.
XX
AC   AAW61197;
XX
DT   07-DEC-1998  (first entry)
XX
DE   Adenovirus death protein.
XX
KW   Adenovirus death protein; ADP; vector; hepatoma; cancer;
KW   alpha-fetoprotein transcription regulatory element; AFP-TRE;
KW   hepatocellular carcinoma; hepatoma; gene therapy; human.
XX
OS   Mastadenovirus type 2.
XX
PN   WO9839465-A2.
XX
PD   11-SEP-1998.
XX
PF   03-MAR-1998;   98WO-US04084.
XX
PR   02-MAR-1998;   98US-0039597.
PR   03-MAR-1997;   97US-0039597.
XX
PA   (CALY-) CALYDON INC.
XX
PI   Henderson DR,  Lamparski HG,  Little AS,  Schuur ER;
XX
DR   WPI; 1998-495861/42.
DR   N-PSDB; AAV47675.
XX
PT   New adenovirus vector, for treating cancers - comprising an
PT   adenovirus gene under the transcriptional control of an alpha
PT   fetoprotein transcription regulatory element
XX
PS   Claim 29; Page 74; 102pp; English.
XX
CC   This is the amino acid of the adenovirus death protein (ADP) of
CC   of adenovirus type 2.  The ADP coding sequence (see AAV47675), with
CC   or without the Y leader, can be introduced into an adenoviral
CC   genome, e.g. in the E3 or E4 region.  Inclusion of such a coding
CC   sequence in an adenoviral vector significantly enhances the extent
CC   of cytotoxicity, cell killing and virus production.  The invention
CC   provides replication-competent adenovirus vectors which
CC   preferentially replicate in cells that express alpha-fetoprotein
CC   (AFP), particularly hepatoma cells.  The vectors comprise at
CC   least one adenovirus gene, preferably a gene that contributes to
CC   cytotoxicity, under the transcriptional control of an AFP
CC   transcription regulatory element (see AAV47654-55).  The vectors
CC   are useful for conferring selective cytotoxicity to AFP-expressing
CC   cells, especially cancer cells.
XX
SQ   Sequence   101 AA;

  Query Match           86.2%;  Score 75;  DB 19;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
```

```
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy     61 CLKRRRARPPIYRPI 75
          |||||||||||||||
Db     61 clkrrrarppiyrpi 75
```

RESULT 6
AAW98003
ID AAW98003 standard; Protein; 101 AA.
XX
AC AAW98003;
XX
DT 21-JUN-1999 (first entry)
XX
DE Adenovirus death protein.
XX
KW Enhancer; glandular kallikrein-1; hGK-1; hKLK2; human;
KW prostate cancer; therapy; adenovirus death protein.
XX
OS Mastadenovirus 2.
XX
PN WO9906576-A1.
XX
PD 11-FEB-1999.
XX
PF 04-AUG-1998; 98WO-US16312.
XX
PR 03-AUG-1998; 98US-0127834.
PR 04-AUG-1997; 97US-0054523.
PR 02-MAR-1998; 98US-0076545.
XX
PA (CALY-) CALYDON INC.
XX
PI Herdenson DR, Schuur ER, Yu D;
XX
DR WPI; 1999-153804/13.
DR N-PSDB; AAX24756.
XX
PT New nucleic acid containing the human glandular kallikrein enhancer
PT - providing increased expression of heterologous sequences in
PT prostatic cells, and related adenoviral vectors for treating
PT prostatic cancer
XX
PS Disclosure; Page 165-166; 179pp; English.
XX
CC This protein comprises the adenovirus death protein (ADP) of
CC adenovirus serotype 2. The invention provides novel adenovirus
CC vectors in which at least one adenovirus gene, preferably one that
CC contributes to cytotoxicity, is placed under transcriptional
CC control of a human glandular kallikrein hKLK2 enhancer
CC transcriptional regulatory element (hKLK2-TRE, see AAX24755). Such
CC vectors are useful for treatment of cancers such as prostate
CC cancer. The ADP gene may render the adenoviral vector more potent,
CC making possible more effective treatment and/or lower dosage
CC requirement.
XX
SQ Sequence 101 AA;

```
  Query Match           86.2%;  Score 75;  DB 20;  Length 101;
  Best Local Similarity 100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy     61 CLKRRRARPPIYRPI 75
          |||||||||||||||
Db     61 clkrrrarppiyrpi 75
```

RESULT 7
AAY84407
ID AAY84407 standard; Protein; 101 AA.
XX
AC AAY84407;
XX
DT 25-JUL-2000 (first entry)
XX
DE Amino acid sequence of an adenoviral death protein.
XX
KW adenoviral vector; adenovirus gene; transcriptional control;
KW transcriptional regulatory element; TRE; adenoviral propagation;
KW death protein; tumour.
XX
OS Mastadenovirus.
XX
PN WO200015820-A1.
XX
PD 23-MAR-2000.
XX
PF 10-SEP-1999; 99WO-US20718.
XX
PR 10-SEP-1998; 98US-0099791.
PR 09-SEP-1999; 99US-0099791.
XX
PA (CALY-) CALYDON INC.
XX
PI Yu DC, Henderson DR;
XX
DR WPI; 2000-271456/23.
DR N-PSDB; AAZ99937.
XX
PT Adenovirus vectors comprising cell-status specific response elements
PT useful in gene therapy protocols for the treatment of cancers -
XX
PS Disclosure; Fig 9; 79pp; English.
XX
CC The present sequence represents an adenoviral death protein, which is
CC used to construct the vectors of the invention. The specification
CC describes adenoviral vectors which comprise an adenovirus gene
CC under transcriptional control of a cell status specific transcriptional
CC regulatory element (TRE). The TRE is preferably one that is
CC essential for adenoviral propagation. The adenovirus vectors
CC may be used for the treatment of a range of tumours such as lung,
CC stomach, breast, colon and rectum, and uterine and cervix cancers.
XX
SQ Sequence 101 AA;

```
  Query Match           86.2%;  Score 75;  DB 21;  Length 101;
  Best Local Similarity 100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy     61 CLKRRRARPPIYRPI 75
          |||||||||||||||
Db     61 clkrrrarppiyrpi 75
```

RESULT 8
AAB47591
ID AAB47591 standard; Protein; 101 AA.
XX
AC AAB47591;
XX
DT 07-JAN-2002 (first entry)
XX
DE ADP amino acid sequence.
XX

KW Adenovirus; ADP; replication-competent; adenoviral vector; TRE;
KW transcriptional regulatory element; mutation; deletion; IRES;
KW promoter; internal ribosome entry site; cytotoxic; cancer; bladder.
XX
OS Adenovirus.
XX
PN WO200173093-A2.
XX
PD 04-OCT-2001.
XX
PF 21-MAR-2001; 2001WO-US09036.
XX
PR 24-MAR-2000; 2000US-192156P.
XX
PA (CALY-) CALYDON INC.
XX
PI Yu D, Li Y, Henderson DR;
XX
DR WPI; 2001-639234/73.
DR N-PSDB; AAH43535.
XX
PT Replication-competent adenoviral vector, useful e.g. for killing cancer
PT cells, contains two genes linked by internal ribosome entry site and
PT controlled by target-specific regulator -
XX
PS Disclosure; Fig 9; 148pp; English.
XX
CC This sequence represents adenoviral ADP. The ADP coding sequence may
CC be used in the replication-competent adenoviral vector (A) of the
CC invention which contains two genes (G1, G2) that are co-transcribed
CC as a single mRNA and under control of a heterologous, target cell-
CC specific transcriptional regulatory element (TRE). G2 has a mutation
CC in, or deletion of, its endogenous promoter and is controlled from
CC an internal ribosome entry site (IRES). The ADP coding sequence may
CC be used as G1 or G2. (A) has greater specificity for a target cell
CC than a similar vector in which TRE is operably linked to a gene and
CC which lacks an IRES. (A) are used to modify the genotype of target
CC cells, optionally in vitro with subsequent return of altered cells to
CC the host and where G2 is a cytotoxic gene, to confer selective
CC cytotoxicity to target cells, especially for killing cancer cells.
CC ADP displays a cytotoxic, particularly cell lysis, function. Also (A)
CC are used for diagnosis and monitoring, e.g. detection of bladder cancer
CC cells. The target cell-specific TRE ensures that (A) has better
CC targeting specificity, with minimal replication in non-target cells, so
CC a runaway infection is prevented but production of adenoviral proteins
CC in target cells activates and/or stimulates the immune response against
CC target cells producing such proteins. The use of an IRES (rather than
CC two identical control elements) eliminates the risk of homologous
CC recombination and may provide enough extra space for an additional
CC (therapeutic) gene.
XX
SQ Sequence 101 AA;

```
  Query Match             86.2%;  Score 75;  DB 22;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy      61 CLKRRRARPPIYRPI 75
           |||||||||||||||
Db      61 clkrrrarppiyrpi 75
```

RESULT 9
AAM50206
ID AAM50206 standard; Protein; 101 AA.
XX
AC AAM50206;
XX
DT 07-JAN-2002 (first entry)
XX
DE Adenovirus death protein.
XX
KW Adenovirus death protein; uroplakin II; vector;
KW transcriptional regulatory element; TRE; urothelial cell;
KW bladder cancer; human; gene therapy.
XX
OS Mastadenovirus 2.
XX
PN WO200172994-A2.
XX
PD 04-OCT-2001.
XX
PF 21-MAR-2001; 2001WO-US09224.
XX
PR 24-MAR-2000; 2000US-191861P.
XX
PA (CALY-) CALYDON INC.
XX
PI Yu D, Zhang H, Henderson DR;
XX
DR WPI; 2001-639229/73.
DR N-PSDB; AAI70186.
XX
PT Human urothelial cell specific uroplakin transcriptional regulatory
PT sequences, useful for producing adenoviral vectors which can be used to
PT confer selective cytotoxicity to target cells, especially bladder
PT cancer cells -
XX
PS Example 6; Fig 12; 147pp; English.
XX
CC The present sequence is that of the adenovirus death protein (ADP).
CC The ADP gene coding region (see AAI70186) was obtained by PCR
CC amplification and used in the construction of adenoviral vectors in
CC which ADP expression was under the control of a urothelial
CC cell-specific transcriptional regulatory element (TRE) derived from
CC the human uroplakin II gene 5' flanking region (see AAI70144). This
CC is an example of adenoviral vectors of the invention. Such vectors
CC comprise a gene, preferably an adenovirus gene, under transcriptional
CC control of a urothelial cell-specific TRE. They display urothelial
CC cell-specific cytotoxicity, and are used for the specific, targeted
CC gene therapy of bladder cancer.
XX
SQ Sequence 101 AA;

```
  Query Match             86.2%;  Score 75;  DB 22;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy      61 CLKRRRARPPIYRPI 75
           |||||||||||||||
Db      61 clkrrrarppiyrpi 75
```

RESULT 10
AAB61866
ID AAB61866 standard; Protein; 101 AA.
XX
AC AAB61866;
XX
DT 08-MAY-2001 (first entry)
XX
DE Ad2 encoded adenovirus death protein (ADP).
XX
KW Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW anti-cancer; gene therapy; cytostatic; Ad2.
XX

```
OS   Mastadenovirus.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..26
FT                   /note= "fragment specifically claimed for"
FT   Domain          1..40
FT                   /note= "putative lumenal domain (AAB61873)"
FT   Domain          41..59
FT                   /note= "transmembrane domain (AAB61874);
FT                    fragment specifically claimed for"
FT   Domain          63..70
FT                   /note= "cytosolic basic proline domain (AAB61875)
FT                    fragment specifically claimed for"
FT   Domain          60..101
FT                   /note= "cytoplasmic-nucleoplasmic domain"
XX
PN   WO200104282-A2.
XX
PD   18-JAN-2001.
XX
PF   12-JUL-2000; 2000WO-US18971.
XX
PR   12-JUL-1999;   99US-0351778.
XX
PA   (UYSL-) UNIV SAINT LOUIS.
XX
PI   Wold WSM,  Toth K,  Doronin K,  Tollefson AE;
XX
DR   WPI; 2001-103079/11.
XX
PT   Recombinant vector which is replication-competent in a neoplastic cell
PT   and overexpresses an adenovirus death protein, useful in cancer therapy
PT   when used together with replication-defective adenovirus which
PT   expresses an anti-cancer gene -
XX
PS   Claim 5; Page 156; 196pp; English.
XX
CC   The invention relates to a recombinant vector (V1) which is replication-
CC   competent in a neoplastic cell and which overexpresses an adenovirus
CC   death protein (ADP). The vector can be used in a method for promoting
CC   death of a neoplastic cell that comprises contacting the neoplastic cell
CC   with at least one V1; and a composition comprising V1 and a second
CC   recombination virus which is: (a) replication defective and which
CC   expresses an anti-cancer gene product, where V1 complements replication
CC   of the second recombinant virus; or (b) replication-competent in a
CC   neoplastic cell. V1, together with one or more replication-defective
CC   adenovirus which expresses an anti-cancer gene product, are useful in
CC   cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC   cells and spread of the virus throughout a cell monolayer than viruses
CC   expressing wild-type levels of ADP. The present sequence represents the
CC   amino acid sequence of an ADP encoded by Ad2.
XX
SQ   Sequence   101 AA;

  Query Match             86.2%;  Score 75;  DB 22;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-68;
  Matches   75;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy      61 CLKRRRARPPIYRPI 75
           |||||||||||||||
Db      61 clkrrrarppiyrpi 75


RESULT  11
AAB61871
ID   AAB61871 standard; Protein; 77 AA.
XX
AC   AAB61871;
XX
DT   08-MAY-2001  (first entry)
XX
DE   Ad2 ADP mutant dl714.
XX
KW   Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW   anti-cancer; gene therapy; cytostatic; Ad2; mutant.
XX
OS   Mastadenovirus.
XX
PN   WO200104282-A2.
XX
PD   18-JAN-2001.
XX
PF   12-JUL-2000; 2000WO-US18971.
XX
PR   12-JUL-1999;   99US-0351778.
XX
PA   (UYSL-) UNIV SAINT LOUIS.
XX
PI   Wold WSM,  Toth K,  Doronin K,  Tollefson AE;
XX
DR   WPI; 2001-103079/11.
XX
PT   Recombinant vector which is replication-competent in a neoplastic cell
PT   and overexpresses an adenovirus death protein, useful in cancer therapy
PT   when used together with replication-defective adenovirus which
PT   expresses an anti-cancer gene -
XX
PS   Example 9; Fig 20; 196pp; English.
XX
CC   The invention relates to a recombinant vector (V1) which is replication-
CC   competent in a neoplastic cell and which overexpresses an adenovirus
CC   death protein (ADP). The vector can be used in a method for promoting
CC   death of a neoplastic cell that comprises contacting the neoplastic cell
CC   with at least one V1; and a composition comprising V1 and a second
CC   recombination virus which is: (a) replication defective and which
CC   expresses an anti-cancer gene product, where V1 complements replication
CC   of the second recombinant virus; or (b) replication-competent in a
CC   neoplastic cell. V1, together with one or more replication-defective
CC   adenovirus which expresses an anti-cancer gene product, are useful in
CC   cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC   cells and spread of the virus throughout a cell monolayer than viruses
CC   expressing wild-type levels of ADP. The present sequence represents the
CC   amino acid sequence of an Ad2 ADP mutant.
XX
SQ   Sequence   77 AA;

  Query Match             80.5%;  Score 70;  DB 22;  Length 77;
  Best Local Similarity   100.0%;  Pred. No. 1.6e-63;
  Matches   70;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLIC 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasldmwwfsialmfvcliimwlic 60

Qy      61 CLKRRRARPP 70
           ||||||||||
Db      61 clkrrrarpp 70


RESULT  12
AAW59925
ID   AAW59925 standard; Protein; 101 AA.
XX
AC   AAW59925;
XX
DT   11-JAN-1999  (first entry)
XX
DE   Adenovirus death protein.
XX
KW   Adenovirus death protein; ADP; transcription regulatory element;
```

```
KW   vector; breast cancer; prostate cancer; liver cancer; colon cancer;
KW   gene therapy.
XX
OS   Mastadenovirus.
XX
PN   WO9839464-A2.
XX
PD   11-SEP-1998.
XX
PF   03-MAR-1998;   98WO-US04080.
XX
PR   02-MAR-1998;   98US-0054523.
PR   03-MAR-1997;   97US-0039762.
PR   03-MAR-1997;   97US-0039763.
PR   04-AUG-1997;   97US-0054523.
XX
PA   (CALY-) CALYDON INC.
XX
PI   Henderson DR,  Lamparski HG,  Yu D;
XX
DR   WPI; 1998-495860/42.
DR   N-PSDB; AAV53632.
XX
PT   New adenovirus vectors, used for treating tumours - comprising first
PT   and second adenovirus genes under control of different heterologous
PT   transcriptional regulatory elements
XX
PS   Disclosure; Page 94; 130pp; English.
XX
CC   This is the amino acid sequence of adenovirus death protein (ADP).
CC   The invention provides replication-competent adenovirus vectors
CC   specific for target cells and methods of using such vectors.  The
CC   vectors contain heterologous transcription regulatory elements
CC   (TREs) and may incorporate a gene, such as the ADP gene (see
CC   AAV53632), which can contribute to cytotoxicity in the target cell.
CC   Adenoviral replication can be restricted to target cells in which
CC   the heterologous TREs are functional and thus the vectors can
CC   provide selective cytotoxicity to the target cells (e.g. prostate,
CC   liver, breast or colon), particularly neoplastic cells.
XX
SQ   Sequence   101 AA;
```

```
  Query Match             59.8%;  Score 52;  DB 19;  Length 101;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-45;
  Matches   52;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      24 LNLPQVHAFVNDWASLDMWWFSIALMFVCLIIMWLICCLKRRRARPPIYRPI 75
           |||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      24 lnlpqvhafvndwasldmwwfsialmfvcliimwlicclkrrrarppiyrpi 75


RESULT  13
AAB61873
ID   AAB61873 standard; Protein; 40 AA.
XX
AC   AAB61873;
XX
DT   08-MAY-2001  (first entry)
XX
DE   Ad2 ADP putative lumenal domain.
XX
KW   Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW   anti-cancer; gene therapy; cytostatic; Ad2.
XX
OS   Mastadenovirus.
XX
PN   WO200104282-A2.
XX
PD   18-JAN-2001.
XX
PF   12-JUL-2000; 2000WO-US18971.
XX
PR   12-JUL-1999;   99US-0351778.
XX
PA   (UYSL-) UNIV SAINT LOUIS.
XX
PI   Wold WSM,  Toth K,  Doronin K,  Tollefson AE;
XX
DR   WPI; 2001-103079/11.
XX
PT   Recombinant vector which is replication-competent in a neoplastic cell
PT   and overexpresses an adenovirus death protein, useful in cancer therapy
PT   when used together with replication-defective adenovirus which
PT   expresses an anti-cancer gene -
XX
PS   Example 9; Fig 20; 196pp; English.
XX
CC   The invention relates to a recombinant vector (V1) which is replication-
CC   competent in a neoplastic cell and which overexpresses an adenovirus
CC   death protein (ADP). The vector can be used in a method for promoting
CC   death of a neoplastic cell that comprises contacting the neoplastic cell
CC   with at least one V1; and a composition comprising V1 and a second
CC   recombination virus which is: (a) replication defective and which
CC   expresses an anti-cancer gene product, where V1 complements replication
CC   of the second recombinant virus; or (b) replication-competent in a
CC   neoplastic cell. V1, together with one or more replication-defective
CC   adenovirus which expresses an anti-cancer gene product, are useful in
CC   cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC   cells and spread of the virus throughout a cell monolayer than viruses
CC   expressing wild-type levels of ADP. The present sequence represents the
CC   amino acid sequence of an Ad2 ADP putative lumenal domain.
XX
SQ   Sequence   40 AA;
```

```
  Query Match             46.0%;  Score 40;  DB 22;  Length 40;
  Best Local Similarity   100.0%;  Pred. No. 2.8e-33;
  Matches   40;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MTGSTIAPTTDYRNTTATGLTSALNLPQVHAFVNDWASLD 40
           ||||||||||||||||||||||||||||||||||||||||
Db       1 mtgstiapttdyrnttatgltsalnlpqvhafvndwasld 40


RESULT  14
AAB61868
ID   AAB61868 standard; Protein; 95 AA.
XX
AC   AAB61868;
XX
DT   08-MAY-2001  (first entry)
XX
DE   Ad6 encoded adenovirus death protein (ADP).
XX
KW   Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW   anti-cancer; gene therapy; cytostatic; Ad6.
XX
OS   Mastadenovirus.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..26
FT                   /note= "fragment specifically claimed for"
FT   Peptide         41..59
FT                   /note= "fragment specifically claimed for"
FT   Peptide         63..70
FT                   /note= "fragment specifically claimed for"
XX
PN   WO200104282-A2.
XX
PD   18-JAN-2001.
XX
PF   12-JUL-2000; 2000WO-US18971.
XX
PR   12-JUL-1999;   99US-0351778.
XX
```

PA (UYSL-) UNIV SAINT LOUIS.
XX
PI Wold WSM, Toth K, Doronin K, Tollefson AE;
XX
DR WPI; 2001-103079/11.
XX
PT Recombinant vector which is replication-competent in a neoplastic cell
PT and overexpresses an adenovirus death protein, useful in cancer therapy
PT when used together with replication-defective adenovirus which
PT expresses an anti-cancer gene -
XX
PS Claim 5; Page 157; 196pp; English.
XX
CC The invention relates to a recombinant vector (V1) which is replication-
CC competent in a neoplastic cell and which overexpresses an adenovirus
CC death protein (ADP). The vector can be used in a method for promoting
CC death of a neoplastic cell that comprises contacting the neoplastic cell
CC with at least one V1; and a composition comprising V1 and a second
CC recombination virus which is: (a) replication defective and which
CC expresses an anti-cancer gene product, where V1 complements replication
CC of the second recombinant virus; or (b) replication-competent in a
CC neoplastic cell. V1, together with one or more replication-defective
CC adenovirus which expresses an anti-cancer gene product, are useful in
CC cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC cells and spread of the virus throughout a cell monolayer than viruses
CC expressing wild-type levels of ADP. The present sequence represents the
CC amino acid sequence of an ADP encoded by Ad6.
XX
SQ Sequence 95 AA;

Query Match 40.2%; Score 35; DB 22; Length 95;
Best Local Similarity 100.0%; Pred. No. 6.9e-28;
Matches 35; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 41 MWWFSIALMFVCLIIMWLICCLKRRRARPPIYRPI 75
||||||||||||||||||||||||||||||||||||
Db 35 mwwfsialmfvcliimwlicclkrrrarppiyrpi 69

RESULT 15
AAB61872
ID AAB61872 standard; Protein; 84 AA.
XX
AC AAB61872;
XX
DT 08-MAY-2001 (first entry)
XX
DE Ad2 ADP mutant dl737.
XX
KW Adenovirus death protein; ADP; neoplastic; cell death; cancer therapy;
KW anti-cancer; gene therapy; cytostatic; Ad2; mutant.
XX
OS Mastadenovirus.
XX
PN WO200104282-A2.
XX
PD 18-JAN-2001.
XX
PF 12-JUL-2000; 2000WO-US18971.
XX
PR 12-JUL-1999; 99US-0351778.
XX
PA (UYSL-) UNIV SAINT LOUIS.
XX
PI Wold WSM, Toth K, Doronin K, Tollefson AE;
XX
DR WPI; 2001-103079/11.
XX
PT Recombinant vector which is replication-competent in a neoplastic cell
PT and overexpresses an adenovirus death protein, useful in cancer therapy
PT when used together with replication-defective adenovirus which
PT expresses an anti-cancer gene -
XX
PS Example 9; Fig 20; 196pp; English.
XX
CC The invention relates to a recombinant vector (V1) which is replication-
CC competent in a neoplastic cell and which overexpresses an adenovirus
CC death protein (ADP). The vector can be used in a method for promoting
CC death of a neoplastic cell that comprises contacting the neoplastic cell
CC with at least one V1; and a composition comprising V1 and a second
CC recombination virus which is: (a) replication defective and which
CC expresses an anti-cancer gene product, where V1 complements replication
CC of the second recombinant virus; or (b) replication-competent in a
CC neoplastic cell. V1, together with one or more replication-defective
CC adenovirus which expresses an anti-cancer gene product, are useful in
CC cancer therapy. Overexpression of ADP by V1 results in faster lysis of
CC cells and spread of the virus throughout a cell monolayer than viruses
CC expressing wild-type levels of ADP. The present sequence represents the
CC amino acid sequence of an Ad2 ADP mutant.
XX
SQ Sequence 84 AA;

Query Match 34.5%; Score 30; DB 22; Length 84;
Best Local Similarity 100.0%; Pred. No. 7.5e-23;
Matches 30; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 46 IALMFVCLIIMWLICCLKRRRARPPIYRPI 75
||||||||||||||||||||||||||||||
Db 29 ialmfvcliimwlicclkrrrarppiyrpi 58

Search completed: June 21, 2002, 08:23:31
Job time: 196 sec